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EVALUATION OF OKRA GUM AS A DRY BINDER IN PARACETAMOL TABLET FORMULATIONS

M.O. EMEJE*, C.Y. ISIMI and O.O. KUNLE
Department of Pharmaceutical Technology and Raw Materials Development, National Institute for Pharmaceutical Research and Development (NIPRD) Idu, P.M.B.21 Garki – Abuja, Nigeria.

ABSTRACT
Okra gum has been evaluated as a binder in paracetamol tablet formulations. Compressional properties of the formulations were analyzed using density measurements and the compression equations of Heckel and Kawakita as assessment parameters. The mechanical properties of the tablets were assessed using the crushing strength and friability of the tablets. Disintegration times of the tablet formulations were assessed using the six station disintegration test apparatus. Formulations containing okra gum as a binder show a faster onset and higher amount of plastic deformation than those containing gelatin. The crushing strength and disintegration times of the tablets increased with increased binder concentration while their friability decreased. Although gelatin produced tablets with higher crushing strength, okra gum produced tablets with longer disintegration times than those containing gelatin. This study suggests that okra gum maybe a useful hydrophilic matrixing agent in sustained drug delivery devices.

KEY WORDS: okra gum, gelatin, paracetamol, mechanical properties, disintegration, compaction characteristics

INTRODUCTION

Binders are important ingredients in the formulation process. They provide the adhesive force required to form powder particles into granules, which in the tabletting process result in the formation of compacts on the application of pressure. Usually the stronger the binder, the higher the compactibility of the tablet, and conversely, the longer the disintegration time of the resulting tablet (Adebayo and Itiola 2003). The film-forming characteristics of polymeric binders are known to influence their distribution over substrates during granulation and in turn determine to a large extent the properties of the resulting granules and tablets (Adebayo and Itiola 2003).

Abelmoschus esculentus is a tall erect annual plant commonly known as 'Okra'. It is widely cultivated in most tropical countries. It can be grown year round and it is known for its viscous mucilaginous solution in water. This properly has been utilized in the production of a plasma expander (Nasipuri et al, 1996). Okra mucilage (OKM) has also been used as a suspending and emulsifying agent (Nasipuri *et al*, 1996; 1999). Recently, the mucilage obtained from Abelmoschus esculentus was reported to have a sustained release property in tablet formulations (Onunkwo and Udeala 2003).

A survey of literature reveals that some physicochemical properties of OKM have been reported (Nasipuri *et al*, 1996). However, it appears that no attempt has been made to study the effects of this gum on the compressional characteristics of tablet formulations. In the present work, a study has been made of the effect of OKM as a binder on the compressional characteristics of a paracetamol tablet formulation in comparison with gelatin using density measurements and the Heckel and Kawakita equations for the analysis of the compression data (Kawakita and Ludde 1970/71; Heckel 1961).

The Heckel equation is the most widely used amongst pharmaceutical scientists (Sonnergaard, 1999) for relating the relative density, D, of a powder led during compression to the applied pressure P. It is expressed as:

$$\ln [1/1 - D] = KP + A \qquad i$$

Table 1 Heckel constants for the paracetamol tablet formulations

Binder type	Binder conc. (%w/w)	Do	Py (KN)	Da	Db
Okra gum	0.0	0.313	1000	0.602	0.289
	0.5	0.259	263	0.505	0.246
	1.0	0.314	147	0.520	0.206
	2.0	0.354	76	0.599	0.245
	3.0	0.407	20	0.651	0.244
	4.0	0.283	122	0.488	0.205
	5.0	0.364	67	0.615	0.251
Gelatin	0.5	0.338	56	0.482	0.144
	1.0	0.299	400	0.646	0.347
	2.0	0.369	250	0.729	0.360
	3.0	0.395	526	0.729	0.334
	4.0	0.349	286	0.702	0.353
	5.0	0.409	154	0.789	0.380

The slope of the linear portion of the curve, K, is the reciprocal of the mean yield pressure, Py, of the material. The intercept of the extrapolated linear region, A, is a function of the original compact volume. It represents two stages of consolidation- one due to the initial relative density of the powder and the other due to densification by particle rearrangement. From the value of A, the relative density Da can be calculated using the following equation;

$$Da = 1 - e^{-A} \qquad \text{ii}$$

The relative density of the powder bed at the point when the applied pressure equals zero, Do, is used to describe the initial rearrangement phase of densification as a result of die filling. The relative density, Db, describes the phase of rearrangement at low pressures and is the difference between Da and Do.

$$Db = Da - Do \qquad \text{iii}$$

The Kawakita equation (Alebiowu and Itiola 2001) is used to study powder compression using the degree of volume reduction, C. The equation describes the relationship between the volume reduction of powder column and the applied pressure;

$$C = [Vo - V/Vo] = [abP/1 + bP] \qquad \text{iv}$$

Where, C, is degree of volume reduction, Vo is Initial volume, V is volume of powder column under the applied pressure P. a, b are constants characteristic to powder being compressed.
The equation above can be re arranged in linear form as:

Table 2: Some properties of the paracetamol granules and tablets.

Binder type	Binder conc. (% w/w)	True density (g/ml)	Hardness (KgF)	Friability (%)	Disintegration (sec)
	0.0	1.41	6.20 ± 2.75	Crumbled	47.20 ± 7.31
	0.5	1.57	6.00 ± 0.45	76.10 ± 41.39	50.46 ± 5.54
	1.0	1.46	4.00 ± 1.01	29.36 ± 41.03	55.85 ± 2.91
Okra gum	2.0	1.23	5.35 ± 0.54	27.15 ± 42.07	73.87 ± 13.67
	3.0	0.98	7.40 ± 1.54	3.96 ± 1.84	107.40 ± 24.83
	4.0	1.51	8.05 ± 2.95	2.17 ± 1.61	109.19 ± 7.70
	5.0	1.20	9.60 ± 2.73	1.91 ± 1.78	124.77 ± 16.20
	0.5	1.27	3.34 ± 0.45	52.18 ± 47.84	4.65 ± 1.42
	1.0	1.37	6.15 ± 1.11	1.80 ± 0.61	18.89 ± 1.91
Gelatin	2.0	1.22	8.65 ± 1.47	1.81 ± 0.63	26.34 ± 5.90
	3.0	1.20	10.75 ± 3.85	0.36 ± 0.62	45.98 ± 9.01
	4.0	1.27	13.95 ± 4.06	1.07 ± 0.62	49.54 ± 13.00
	5.0	1.14	19.60 ± 4.01	0.72 ± 0.72	55.89 ± 7.72

$$P/C = P/a + 1/ab \qquad v$$

From the graphical presentation of P/C versus P, the constants maybe evaluated. The constant a, is given as a reciprocal of the slope from the linear portion of the plot and equivalent to the value of C at infinitely high pressures. 1/ab is the intercept. a, gives an indication of the maximum volume reduction available and is considered to describe the compressibility of a powder, while b is considered to describe an inclination toward volume reduction. However, the actual physical meaning of the constants a and b have been in question (Alderborn and Nystrom 1995). Consequently, Kawakita *et al* (Kawakita *et al*, 1983) have applied another equation in describing the volume reduction on tapping and vibrating processes, where the pressure P, is replaced by the tapping number, N.;

$$N/C = [(1/a)\ N \div 1/ab] \qquad vi$$

Where, N is the tapping number, C is the degree of volume reduction and a and b are constants .C in equation vi is given by;

$$C = [Vo - V_N] \div Vo \qquad vii$$

Where Vo is the initial apparent volume and VN, the volume at tapping number N. The constants of Kawakita equation can be used to estimate the flow and cohesiveness properties of powders. Constant a describes the compressibility and constant 1/b describes cohesive properties of powders or the fastness of how the final packing stage is achieved (Kawakita *et al*, 1983).

MATERIAL AND METHODS

Materials

Abelmoschus esculentus mucilage (OKM), lactose (sigma-Aldrich, Chemic GmbH, Germany), Paracetamol BP was obtained from NIPCO pharmaceuticals (Nigeria) and Gelatin obtained from fisons scientific apparatus, (Lough borough, England).

Method

Extraction and Purification of OKM

OKM was extracted and purified as previously described by Nasipuri *et al* (Nasipuri *et al* 1996).

Table 3: parameters obtained from kawakita plots for paracetamol tablet formulations.

Binder type	Binder conc. (% w/w)	1/ab	1/a	A	1/b
Okra gum	0.0	11.73	5.87	0.170	1.99
	0.5	10.30	5.48	0.182	1.88
	1.0	16.39	4.30	0.233	3.81
	2.0	13.60	4.40	0.227	3.09
	3.0	9.67	4.09	0.244	2.36
	4.0	17.14	4.50	0.222	3.81
	5.0	14.14	4.95	0.202	2.86
Gelatin	0.5	20.16	3.45	0.290	5.84
	1.0	20.59	3.08	0.325	6.69
	2.0	16.34	3.74	0.267	4.37
	3.0	37.60	2.50	0.400	15.04
	4.0	10.47	4.16	0.240	2.52
	5.0	19.25	4.01	0.249	4.80

Preparation of granules

Dried powdered OKM or gelatin equivalent to 0, 0.5, 1.0, 2.0 3.0, 4.0 and 5.0% w/w was mixed with paracetamol powder respectively and made up with lactose BP. The mixture was blended thoroughly in a tumbler mixer for 10mins and granulated with water in a granulator (Erweka, Germany) fitted with a 1.7mm sieve the granules were dried in a hot air oven at 60^{O}C for 1 hour.

Preparation and Evaluation of compacts

Compacts equivalent to 500mg paracetamol were produced by compressing the granules for 60 seconds with predetermined loads (at various compression pressures) using a manesty tableting machine (Shangai, China). 50 tablets were compressed at each pressure. All readings are average of 3 measurements. Before each compression, the die (12.5mm in diameter) and flat faced punches were lubricated with a 1% w/v dispersion of magnesium stereate in chloroform. After ejection, the tablets were stored over silica gel in a dessicator for 24 hours to allow for elastic recovery and hardening to prevent falsely low yield values (Krycer *et al*, 1982) and the dimensions of the compact were determined using the mitutoyo model IDC1012EB (Mitutuyo corporation, Japan) thickness gauge to the nearest 0.01mm. The Heckel and Kawakita Plots were statistically analysed using the Microsoft Excel computer software.

The relative density of the compacts was calculated using the equation;

$$D = \frac{w}{Vt} \times \rho s \quad \text{---------- (7)}$$

Where w is the weight of the compact (g), Vt is the volume of the compact (cm^3), and ρs is the density of granules ($glcm^3$). The crushing strength of the compacts was determined using an Erweka hardness tester (Erweka, GmbH, Germany). Ten tablets were tested at each compression pressure. Disintegration time of compacts were determined in 0.IN HCL at 37 ± 0.5^{0}C in a BP disintegration test unit (Manesty Machines, Poole, UK).

RESULTS AND DISCUSSION

Table 1 shows the physical properties of paracetamol granules and tablets containing various concentrations of the OKM and gelatin. The results indicate that compact hardness increased with increased binder concentration except between 0.5 and 2.0 % w/w OKM concentration. This increase indicates the formation of stronger bonds. At all concentrations between 2 and 5 %w/w, tablets made of gelatin as binder exhibited higher crushing strength indicating that gelatin as a binder forms stronger bonds than OKM. Compacts containing gelatin as binder were less

friable than those with OKM. The lower concentration of OKM produced highly friable tablets although the tablets had fairly good hardness. This would seem to imply that the bonds formed were fragile.

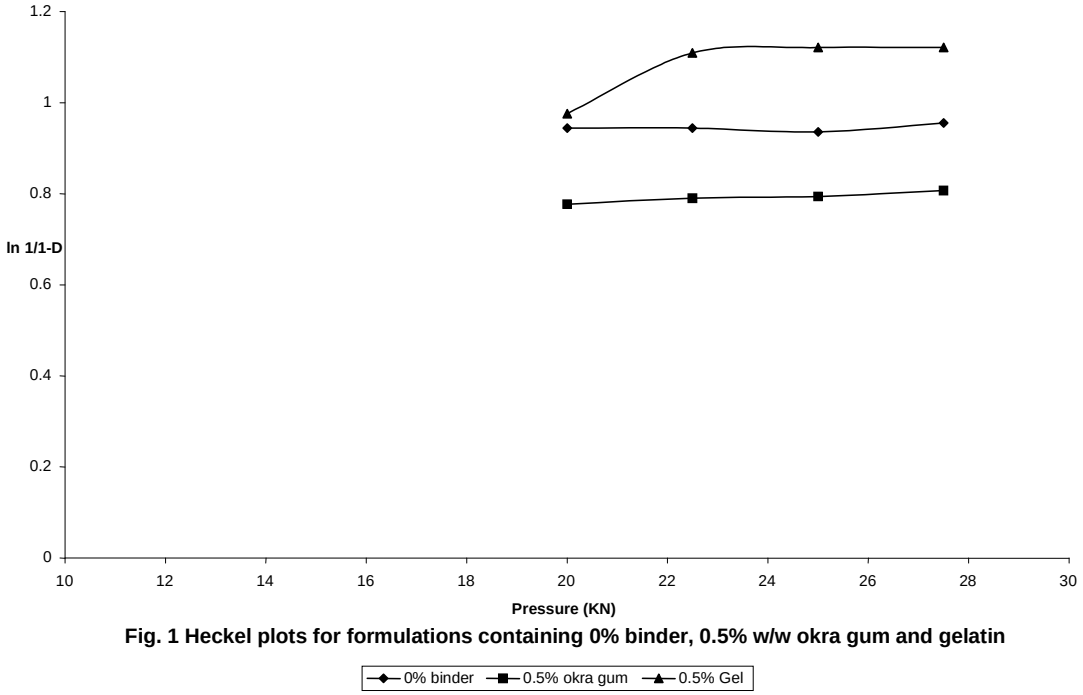

Fig. 1 Heckel plots for formulations containing 0% binder, 0.5% w/w okra gum and gelatin

Except for the 0.5 % gelatin, disintegration time increased with increase in binder concentration. This effect was more pronounced with OKM, which also produced compacts with relatively longer disintegration time. It was also observed that despite the relatively low hardness, and high friability, the disintegration time of OKM containing compacts was much higher than those of gelatin especially at the high concentration levels.

Compaction characteristics

Figure 1 shows representative Heckel plots for paracetamol formulations containing 0 and 0.5% w/w OKM or gelatin as binders. While gelatin increased the compressibility of the granules relative to the formulation without a binder, OKM decreased it. The values of Py, Da, Db, and Do for all the formulations are presented in table II.

All the batches with binder had higher Do values than the control batch without binder, which is an indication that the extent of initial packing of the granules due to die filling decreased on the addition of binder. The exceptions to this were OKM at 0.5 and 4.0%. Generally, gelatin was found to facilitate initial packing of the granules better than OKM.

OKM decreased the Db values of the granules relative to the control (0% binder), while gelatin had the opposite effect except at 0.5%.This implies that the extent of rearrangement of particles at low pressure was lower with OKM. All of these would explain the fact that Da value for OKM was lower between 1.0 and 5.0% w/w indicating

lower packing at zero and lower pressures. The Db values for formulations containing OKM were much lower than their Do values, suggesting that higher pressures are required for granule fragmentation.

The values of Da representing the total degree of packing achieved at zero and low pressures were generally lower for formulations containing OKM between 1.0 and 5.0 % w/w, these values were observed to increase with increase in binder concentration.

The mean yield pressure is inversely related to the ability of a material to deform plastically under pressure. The values of Py for the formulations containing both binders were lower than for the formulations without a binder implying that the presence of binders increased the plasticity of the formulation. The Py values for formulations containing OKM were lower than those containing gelatin except at 0.5%w/w concentration. This implies that the onset of plastic deformation in the formulations containing OKM occurred at lower pressures. The values of Py also decrease with increase in the concentration of OKM between 0.5 and 3%w/w. No particular trend was however

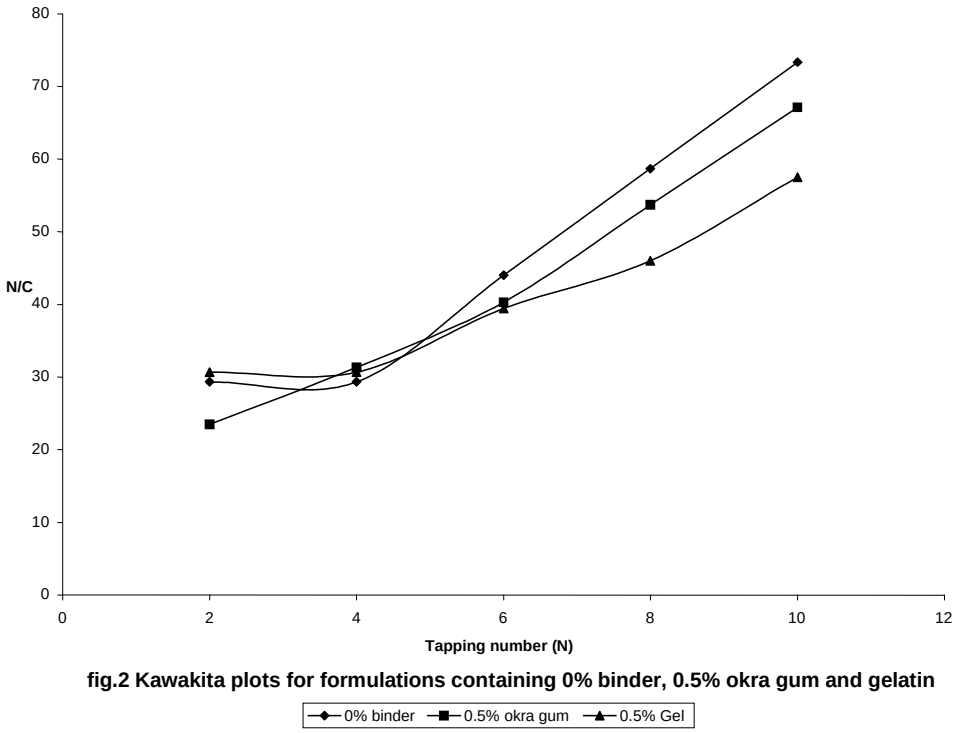

fig.2 Kawakita plots for formulations containing 0% binder, 0.5% okra gum and gelatin

observed for formulations containing gelatin. It is notable that the formulations contain 3%w/w gelatin exhibited the highest values.

The Py values of the formulations without a binder was rather high (1000KN) compared with what could be expected from an 83.33% formulation of paracetamol – Py of pure paracetamol reported by others to be 96.9 and 110MNm-2 (Alebiowu and Itiola 2001). Other authors have reported a similar observation (Alebiowu and Itiola 2001).This phenomenon has been attributed to the complex nature of a formulation containing more than one component.

Figure 2 shows representative kawakita plots for paracetamol formulations containing 0 and 0.5%w/w binders, where almost a linear relationship between N/C and N was obtained. However, the degree of volume reduction C,

changes with change in tapping number. This initial change in C, was more rapid in formulations without a binder, followed by those with OKM and then gelatin. Formulation containing 0.5%w/w OKM exhibited better linearity with correlation coefficient values of 0.99 than formulations containing no or 0.5%w/w gelatin with correlation coefficient value of 0.44 and 0.93 respectively. The tapping experiments are performed on all samples and a and 1/b are evaluated. Table 3 shows the Kawakita constants. It is observed from this table that values of a are generally larger in formulations containing gelatin than in formulations containing OKM, therefore, their fluidities are worse. It is predicted that the cohesiveness of the formulations containing gelatin would increase, because, 1/b is large in these formulations.

Low values of 1/b indicate materials that are soft and that readily deform plastically under pressure. Table 3 did not show any particular trend in the values of 1/b. Formulations containing 0.5%w/w OKM exhibited the lowest value of 1/b, while formulations containing 3%w/w gelatin exhibited the highest 1/b value.

CONCLUSIONS

The results presented here shows that the mucilage obtained from Abelmoschus esculentus can be used as a binder in paracetamol tablet formulation with good physical properties. Tablets of long disintegration times were produced, hence its potential in sustained released formulations. From the result obtained, OKM compared favorably with the standard gelatin as a binder.

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Corresponding Author:
M.O. EMEJE
Department of Pharmaceutical Technology and Raw Materials Development, National Institute for Pharmaceutical Research and Development (NIPRD) Idu, P.M.B.21 Garki – Abuja, Nigeria.
Phone number; +234092902619
Fax number; 234-9-5239089
Email; martinsemeje@yahoo.com